AF 5/3/07

AMENDMENT UNDER 37 C.F.R. § 1.116
Appln. No.: 09/674,377

Docket No: Q61434

Do Not Enter 6/7/07

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

LISTING OF CLAIMS:

Claim 1. (Currently amended): A neovascularization inhibitor comprising the following polypeptide (a) or (b) as an active ingredient:

(a) a polypeptide ~~having the amino acid sequence PyrGlu^{32} to Val^{478} of human hepatocyte growth factor (HGF)~~ having the amino acid sequence of SEQ ID NO: 1; or

(b) a polypeptide ~~having an amino acid sequence derived from the amino acid sequence of (a) by the deletion, substitution or addition of one or several amino acids and having antagonistic activity against the c-Met/HGF receptor-mediated action of HGF~~ having the amino acid sequence of SEQ ID NO: 2;

wherein ~~the polypeptide of (a) and (b) has a deletion of amino acids 162-166 of human HGF~~ each of polypeptides (a) and (b) has at least one hairpin domain and four Kringle domains.

Claim 2. (Currently amended): ~~A neovascularization inhibitor~~ The neovascularization inhibitor according to claim 1, comprising the polypeptide having the amino acid sequence of SEQ ID NO: 2, wherein the polypeptide having the amino acid sequence of SEQ ID NO: 2 has at least one hairpin domain and four Kringle domains ~~the following polypeptide (a) or (b) as an active ingredient:~~

~~(a) a polypeptide having the amino acid sequence PyrGlu^{32} to Val^{478} of human hepatocyte growth factor (HGF); or~~

~~(b) a polypeptide having an amino acid sequence derived from the amino acid sequence defined in (a) by the deletion, substitution or addition of one or several amino acids, and having antagonistic activity against the c-Met/HGF receptor-mediated action of HGF and inhibitory action against the growth of vascular endothelial cells induced by bFGF and/or VEGF;~~

~~wherein the polypeptide of (a) and (b) has a deletion of amino acids 162-166 of human HGF~~.

Claim 3. (Canceled)

Claim 4. (Previously presented): The neovascularization inhibitor as set forth in claim 1 or 2, wherein said polypeptide is obtainable by elastase digestion of human hepatocyte growth factor harboring a deletion of amino acids 162-166.

Claim 5. (Canceled)

Claim 6. (Currently amended): A neovascularization inhibitor composition comprising the polypeptide ~~defined by~~ having the amino acid sequence of SEQ ID NO: 2 and a pharmaceutically acceptable carrier.

Claims 7-11. (Canceled)

Claim 12. (Currently amended): A method of inhibiting neovascularization which comprises administering to a subject in need of such treatment a neovascularization inhibitor composition comprising the following polypeptide (a) or (b) and a pharmaceutically acceptable carrier:

(a) a polypeptide ~~having the amino acid sequence PyrGlu^{32} to Val^{478} of human hepatocyte growth factor (HGF)~~ having the amino acid sequence of SEQ ID NO: 1; or

(b) a polypeptide ~~having an amino acid sequence derived from the amino acid sequence defined in (a) by the deletion, substitution or addition of one or several amino acids and having antagonistic activity against the c-Met/HGF receptor-mediated action of HGF~~ having the amino acid sequence of SEQ ID NO: 2;

wherein ~~the polypeptide of (a) and (b) has a deletion of amino acids 162-166 of human HGF~~ each of polypeptides (a) and (b) has at least one hairpin domain and four Kringle domains.

Claim 13. (Currently amended): A method of inhibiting neovascularization which comprises administering to a subject in need of such treatment a neovascularization inhibitor composition comprising the following polypeptide (a) or (b) and a pharmaceutically acceptable carrier:

(a) a polypeptide ~~having the amino acid sequence PyrGlu^{32} Val^{478} of human hepatocyte growth factor (HGF)~~ having the amino acid sequence of SEQ ID NO: 1; or

(b) a polypeptide ~~having an amino acid sequence derived from the amino acid sequence defined in (a) by the deletion, substitution or addition of one or several amino acids, and having antagonistic activity against the c-Met/HGF receptor-mediated action of HGF and inhibitory action against the growth of vascular endothelial cells induced by bFGF and/or VEGF~~ having the amino acid sequence of SEQ ID NO: 2;

wherein ~~the polypeptide of (a) and (b) has a deletion of amino acids 162-166 of human HGF~~ each of polypeptides (a) and (b) has at least one hairpin domain and four Kringle domains.

Claim 14. (Currently amended): A method for treating a disease associated with abnormal angiopoiesis which comprises administering, to a subject in need of such treatment, a neovascularization inhibitor composition comprising the following polypeptide (a) or (b) and a pharmaceutically acceptable carrier:

(a) a polypeptide ~~having the amino acid sequence PyrGlu^{32} to Val^{478} of human hepatocyte growth factor (HGF)~~ having the amino acid sequence of SEQ ID NO: 1; or

(b) a polypeptide ~~having an amino acid sequence derived from the amino acid sequence defined in (a) by the deletion, substitution or addition of one or several amino acids and having antagonistic activity against the c-Met/HGF receptor-mediated action of HGF~~ having the amino acid sequence of SEQ ID NO: 2;

wherein ~~the polypeptide of (a) and (b) has a deletion of amino acids 162-166 of human HGF~~ each of polypeptides (a) and (b) has at least one hairpin domain and four Kringle domains.

Claim 15. (Currently amended): A method for treating a disease associated with abnormal angiopoiesis which comprises administering, to a subject in need of such treatment, a neovascularization inhibitor composition comprising the following polypeptide (a) or (b) and a pharmaceutically acceptable carrier:

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(a) a polypeptide ~~having the amino acid sequence PyrGlu^{32} [[-]]to Val^{478} of human hepatocyte growth factor (HGF)~~ having the amino acid sequence of SEQ ID NO: 1; or

(b) a polypeptide ~~having an amino acid sequence derived from the amino acid sequence defined in (a) by the deletion, substitution or addition of one or several amino acids, and having antagonistic activity against the c-Met/HGF receptor-mediated action of HGF and inhibitory action against the growth of vascular endothelial cells induced by bFGF and/or VEGF~~ having the amino acid sequence of SEQ ID NO: 2;

wherein ~~the polypeptide of (a) and (b) has a deletion of amino acids 162-166 of human HGF~~ each of polypeptides (a) and (b) has at least one hairpin domain and four Kringle domains.

Claim 16. (Withdrawn-Previously presented): The method of claim 14 or 15, wherein said disease is any disease selected from the group consisting of rheumatoid arthritis, psoriasis, Osler-Webber syndrome, myocardial angiopoiesis, telangiectasia, hemophilic joint, angiogenic diseases of the eye, angiofibroma, benign tumors, wound granulation, enteric adhesion, Crohn's disease, atherosclerosis, scleroderma and overcicatrization.

Claims 17-19. (Canceled)

Claim 20. (previously presented): A pharmaceutical composition comprising, as an active ingredient, a polypeptide having the amino acid sequence of SEQ ID NO: 2.

Claims 21-27. (Canceled)

Claim 28. (Currently amended): A method for treating a solid cancer and/or cancer metastasis, which comprises administering to a subject in need of such treatment a pharmaceutical composition containing the following polypeptide (a) or (b):

(a) a polypeptide ~~having the amino acid sequence PyrGlu^{32} - Val^{478} of human hepatocyte growth factor (HGF)~~ having the amino acid sequence of SEQ ID NO 1; or

(b) a polypeptide ~~having an amino acid sequence derived from the amino acid sequence defined in (a) by the deletion, substitution or addition of one or several amino acids~~ having the amino acid sequence of SEQ ID NO: 2;

wherein ~~the polypeptide of (a) and (b) has a deletion of amino acids 162-166 of human HGF~~ each of polypeptides (a) and (b) has at least one hairpin domain and four Kringle domains.

Claim 29. (Currently amended): A method for treating a solid cancer and/or cancer metastasis, which comprises administering to a subject in need of such treatment a pharmaceutical composition containing the polypeptide ~~having an amino sequence defined by~~ having the amino acid sequence of SEQ ID NO: 2.

Claim 30. (Previously presented): The method as claimed in Claim 28 or Claim 29, wherein said subject has a lung cancer or mammary cancer.

Claim 31. (Currently amended) A method for inhibiting tumor growth or metastasis, which comprises administering to a subject in need of such treatment a pharmaceutical composition containing the following polypeptide (a) or (b):

(a) a polypeptide ~~having the amino acid sequence PyrGlu^{32} to Val^{478} of human hepatocyte growth factor (HGF)~~ having the amino acid sequence of SEQ ID NO: 1; or

(b) a polypeptide ~~having an amino acid sequence derived from the amino acid sequence defined in (a) by the deletion, substitution or addition of one or several amino acids~~ having the amino acid sequence of SEQ ID NO: 2;

wherein ~~the polypeptide of (a) and (b) has a deletion of amino acids 162-166 of human HGF~~ each of polypeptides (a) and (b) has at least one hairpin domain and four Kringle domains.

Claim 32. (Currently amended): A method for inhibiting tumor growth ormetastasis, which comprises administering to a subject in need of such treatment a pharmaceutical composition containing the polypeptide ~~having an amino acid sequence defined by~~ having the amino acid sequence of SEQ ID NO: 2.

Claim 33. (Previously presented): The method for inhibiting tumor growth or metatasis as claimed in Claim 31 or Claim 32, wherein the subject has lung cancer or mammary cancer.

Claim 34. (Currently amended): A method for treating a disease arising from vascular hyperplasia and/or caused by an excessive or abnormal stimulation of the endothelial cells, which comprises administering to a subject in need of such treatment a pharmaceutical composition containing the following polypeptide (a) or (b):

(a) a polypeptide ~~having the amino acid sequence PyrGlu^{32} to Val^{478} of human hepatocyte growth factor (HGF)~~ having the amino acid sequence of SEQ ID NO: 1; or

(b) a polypeptide ~~having an amino acid sequence derived from the amino acid sequence defined in (a) by the deletion, substitution or addition of one or several amino acids~~ having the amino acid sequence of SEQ ID NO: 2;

wherein ~~the polypeptide of (a) and (b) has a deletion of amino acids 162-166 of human HGF~~ each of polypeptides (a) and (b) has at least one hairpin domain and four Kringle domains.

Claim 35. (Currently amended) A method for treating a disease arising from vascular hyperplasia or/and caused by an excessive or abnormal stimulation of the endothelial cells, which comprises administering to a subject in need of such treatment a pharmaceutical composition containing the polypeptide ~~having an amino acid sequence defined by~~ having the amino acid sequence of SEQ ID NO: 2.

Claim 36. (Previously presented): The method of Claim 34 or Claim 35, wherein said disease is a disease selected from the group consisting of rheumatoid arthritis, psoriasis, Osler Webber syndrome, myocardial angiopoiesis, telangiectasia, hemophilic joint, angiogenic diseases of the eyes, angiofibroma, benign tumors, hematopoietic malignancies, wound granulation, enteric adhesion, Crohn's disease, atherosclerosis, scleroderma and over cicatrization.

Claim 37. (Withdrawn-Currently amended): A method for controlling conception which comprises administering to a subject a pharmaceutical composition comprising the following polypeptide (a) or (b):

(a) a polypeptide ~~having the amino acid sequence PyrGlu^{32}-Val^{478} of human hepatocyte growth factor (HGF)~~ having the amino acid sequence of SEQ ID NO: 1; or

(b) a polypeptide ~~having an amino acid sequence derived from the amino acid sequence defined in (a) by the deletion, substitution or addition of one or several amino acids~~ having the amino acid sequence of SEQ ID NO: 2;

wherein ~~the polypeptide of (a) and (b) has a deletion of amino acids 162-166 of human HGF~~ each of polypeptides (a) and (b) has at least one hairpin domain and four Kringle domains.